# Natural compounds: Docking, pharmacokinetics, interactions.

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## Introduction

The exploration of natural compounds as therapeutic agents and their potential to interact with existing medications is a significant area of pharmacological research, heavily leveraging computational methods. Initial investigations have, for instance, employed molecular docking to identify natural compounds derived from Buxus sempervirens L. as promising inhibitors of the SARS-CoV-2 Main Protease. These studies concurrently evaluated the pharmacokinetic properties of these compounds to predict their absorption, distribution, metabolism, excretion, and toxicity (ADMET) profiles, ultimately suggesting candidates with favorable drug-likeness for further development [1].

Another broader perspective highlights the critical role of natural products in modulating CYP450 enzymes, which are central to drug metabolism. A comprehensive review extensively examined various natural compounds for their ability to affect these enzymes, shedding light on potential drug-drug interactions. Through molecular docking simulations, researchers elucidated the precise binding mechanisms, providing invaluable insights into their pharmacokinetic behavior and broader therapeutic implications [2].

Understanding these complex interactions often requires an integrated approach. One paper explored drug-drug interactions involving natural products by combining in vitro, in vivo, and in silico methodologies, notably including molecular docking. This multifaceted strategy offers a comprehensive understanding of how natural compounds can significantly alter drug pharmacokinetics, thereby providing essential guidance for developing safer co-administration practices in clinical settings [3].

Further contributing to this understanding, specific phytochemicals from Curcuma longa L. have been rigorously investigated using molecular docking and pharmacokinetic prediction. This research aimed to identify their potential as inhibitors of human cytochrome P450 enzymes. The findings detailed specific compounds possessing favorable binding affinities and advantageous ADMET profiles, strongly indicating their capacity to instigate meaningful drug interactions [4].

The discussion extends to natural products that modulate P-glycoprotein, a pivotal efflux transporter. A comprehensive review meticulously examined the role of these natural compounds in overcoming multidrug resistance and their profound influence on drug pharmacokinetics. The discussion intricately covers the molecular mechanisms, frequently substantiated by detailed docking studies, that underpin these interactions and highlight their substantial therapeutic potential [5].

In parallel, a study specifically focused on natural compounds extracted from Garcinia kola seeds, utilizing a combination of molecular docking and pharmacokinetic evaluation to assess their potential as P-glycoprotein inhibitors. This investigation successfully identified compounds exhibiting strong binding affinities and favorable ADME profiles, suggesting their crucial role in influencing drug transport and indicating a tangible potential for herb-drug interactions [6].

The utility of computational tools is further underscored by a review focusing on in silico methods, including molecular docking, for accurately predicting drug-drug interactions between various natural products and cytochrome P450 enzymes. This work emphasized the profound importance of these sophisticated computational approaches in deciphering the pharmacokinetic basis of herb-drug interactions, thereby significantly aiding in risk assessment and fostering safer drug development pipelines [7].

Beyond drug interaction studies, research has also applied these methodologies to therapeutic discovery. One notable study investigated the pharmacokinetics and performed molecular docking for selected natural products specifically targeting breast cancer. The primary objective was to identify compounds with favorable ADMET profiles and robust binding affinities to key cancer targets, offering critical insights into their utility as novel therapeutic agents, while concurrently considering their interaction profiles [8].

The assessment of metabolic enzyme inhibition by natural products extends to other critical pathways. Molecular docking, ADME, and toxicity predictions were employed to evaluate bioactive compounds derived from Azadirachta indica as potential inhibitors of human UDP-Glucuronosyltransferases (UGTs). This particular study successfully identified natural products capable of altering drug metabolism through UGT inhibition, thus foregrounding po-

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tential pharmacokinetic drug interactions that warrant clinical consideration [9].

Rounding out these investigations, the pharmacokinetics and molecular docking of specific phytochemicals obtained from Artemisia annua were explored regarding their potential as P-glycoprotein inhibitors. The findings from this research strongly suggest that certain compounds possess the ability to modulate P-glycoprotein activity, an effect that could significantly impact drug absorption and elimination, thereby indicating a clear potential for pharmacokinetic drug interactions [10].

## Conclusion

The compiled research extensively utilizes molecular docking alongside pharmacokinetic studies to investigate the therapeutic potential and interaction profiles of natural compounds. These studies explore diverse plant sources like Buxus sempervirens L. [1], Curcuma longa L. [4], Garcinia kola [6], and Artemisia annua [10], aiming to identify novel inhibitors for critical biological targets. Key targets include the SARS-CoV-2 Main Protease [1], various human cytochrome P450 enzymes involved in drug metabolism [2, 4, 7], and P-glycoprotein, a significant efflux transporter implicated in multidrug resistance [5, 6, 10]. A consistent theme across these investigations is the evaluation of ADMET (Absorption, Distribution, Metabolism, Excretion, Toxicity) properties, which are crucial for predicting the drug-likeness and safety of potential drug candidates. This predictive analysis provides essential insights into how natural compounds might influence overall drug pharmacokinetics and highlights their propensity for causing drug-drug or herb-drug interactions. Researchers also employed integrated strategies, combining in vitro, in vivo, and in silico methods, to gain a comprehensive understanding of how natural compounds alter drug pharmacokinetics [3]. Specific examples include assessing bioactive compounds from Azadirachta indica for their inhibitory effects on human UDP-Glucuronosyltransferases [9] and evaluating natural products against breast cancer targets [8]. Together, this body of work illustrates the robust application of computational methodologies in pharmacology, underscoring their importance in the early stages of drug discovery, risk assessment, and guiding safer co-administration practices for natural products.

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